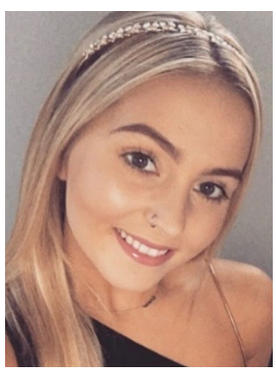

Understanding the mechanisms of cardiovascular diseases involving amyloid protein aggregation

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Proteins can enter an “amyloid state”, consisting of elongated fibres with β-pleated sheets; amyloid fibrils form due to the aggregation of misfolded proteins. When the cause of a disease involves amyloid proteins they are often, but not always, known as “amyloidosis” diseases; these can be systematic, affecting the whole body, or localised pathologies, affecting only specific tissues.

Research into the role of amyloid proteins in Prion disease and Alzheimer’s disease is in abundance and the mechanism is generally well understood. However, few discoveries have been made into the role of amyloid proteins in cardiac disease. Cardiac amyloidosis is most commonly characterised by the thickening of the walls of the heart, disrupting the architecture of the cardiac tissue. Ultimately, cardiac amyloidosis results in cardiac dysfunction and failure. Usually, multiple proteins are found to be aggregated in amyloidosis diseases which, based on the Prion hypothesis, is thought to reduce the time taken for amyloid fibril formation and therefore affect further aggregation of proteins.

This project will investigate four proteins found aggregated in the cardiovascular system - medin, apolipoprotein AI, transthyretin and light chains. To do this we will perform a cross-seeding experiment, which involves introducing a misfolded form of one protein to a different normally folded protein and determining if the time taken for amyloid fibrils to form has reduced. With this research, the mechanisms of cardiac amyloidosis will hopefully be elucidated allowing for the identification of potential therapeutic targets for the disease.